SEOUENCE LISTING

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<110> Co, Man Sung
     Vasquez, Maximiliano
      Carreno, Beatriz
      Celniker, Abbie Cheryl
      Collins, Mary
      Goldman, Samuel
     Gray, Gary S.
      Knight, Andrea
      O'Hara, Denise
      Rup, Bonita
      Veldman, Geertruida M.
<120> HUMANIZED IMMUNOGLOBULIN REACTIVE WITH B7-2 MOLECULES AND
METHODS OF TREATMENT THEREWITH
<130> 08702.0081-00000
<140> 09/249,011
<141> 1999-02-12
<160> 52
<170> PatentIn version 3.1
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48
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                                    10
gtg cac tcc cag gtc cag ctg cag cag tct ggg cct gag ctg gtg agg
Val His Ser Gln Val Gln Leu Gln Gln Ser Glv Pro Glu Leu Val Arg
            20
                                25
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cct ggg gaa tca gtg aag att tcc tgc aag ggt tcc ggc tac aca ttc 144 Pro Gly Glu Ser Val Lys Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe act gat tat gct ata cag tgg gtg aag cag agt cat gca aag agt cta Thr Asp Tyr Ala Ile Gln Trp Val Lys Gln Ser His Ala Lys Ser Leu gag tgg att gga gtt att aat att tac tat gat aat aca aac tac aac Glu Trp Ile Gly Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn 65 8.0 cag aag ttt aag ggc aag gcc aca atg act gta gac aaa tcc tcc agc 288 Gln Lvs Phe Lvs Glv Lvs Ala Thr Met Thr Val Asp Lvs Ser Ser Ser 85 90 95 aca qcc tat atq qaa ctt qcc aqa ttq aca tct qaq gat tct qcc atc Thr Ala Tyr Met Glu Leu Ala Arg Leu Thr Ser Glu Asp Ser Ala Ile tat tac tgt gca aga gcg gcc tgg tat atg gac tac tgg ggt caa gga 384 Tyr Tyr Cys Ala Arg Ala Ala Trp Tyr Met Asp Tyr Trp Gly Gln Gly acc tca qtc acc qtc tcc tca 405 Thr Ser Val Thr Val Ser Ser 130 135 <210> 2 <211> <212> PRT <213> Murine anti-B7-2 heavy chain <400> 2 Met Gly Trp Asn Cys Ile Ile Phe Phe Leu Val Thr Thr Ala Thr Gly 1

Val His Ser Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Arg 20 25 30

Thr Asp Tyr Ala Ile Gln Trp Val Lys Gln Ser His Ala Lys Ser Leu $50 \hspace{1.5cm} 55 \hspace{1.5cm} 60 \hspace{1.5cm}$

Glu Trp Ile Gly Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn 65 70707580

Gln Lys Phe Lys Gly Lys Ala Thr Met Thr Val Asp Lys Ser Ser Ser Ser 90 \$95\$

Thr Ala Tyr Met Glu Leu Ala Arg Leu Thr Ser Glu Asp Ser Ala Ile $100 \\ 105 \\ 110$

Tyr Tyr Cys Ala Arg Ala Ala Trp Tyr Met Asp Tyr Trp Gly Gln Gly
115 120 125

Thr Ser Val Thr Val Ser Ser 130 135

<210> 3

<211> 396

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<222> (1)..(396)

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atg gat toa cag goo cag gtt ott ata t
tg otg otg ota t
gg gta tot $48\,$

Met Asp Ser Gln Ala Gln Val Leu Ile Leu Leu Leu Leu Trp Val Ser 1 10 15 ggt acc tqt ggg gac att qtg ctg tca cag tct cca tcc tcc ctg gct 96 Gly Thr Cys Gly Asp Ile Val Leu Ser Gln Ser Pro Ser Ser Leu Ala 30 gtg tca gca gga gag aag gtc act atg agc tgc aaa tcc agt cag agt 144 Val Ser Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser ctq ctc aac agt aga acc cga gag aac tac ttg gct tgg tac cag cag 192 Leu Leu Asn Ser Arg Thr Arg Glu Asn Tvr Leu Ala Trp Tvr Gln Gln 60 aaa cca ggg cag tot cot aaa ctg ctg atc tac tgg gca toc act agg 240 Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg 65 75 80 gaa tot ggg gto cot gat ogc tto aca ggo agt gga tot ggg aca gat Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp 85 90 95 ttc act ctc acc atc agc agt gtg cag gct gaa gac ctg gca gtt tat Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr tac tgc acg caa tct tat aat ctt tac acg ttc gga ggg ggg acc aag 384 Tyr Cys Thr Gln Ser Tyr Asn Leu Tyr Thr Phe Gly Gly Gly Thr Lys 120 ctq qaa ata aaa 396 Leu Glu Ile Lys

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<213> Murine anti-B7-2 light chain

<400> 4

Met Asp Ser Gln Ala Gln Val Leu Ile Leu Leu Leu Leu Trp Val Ser $1 \hspace{1.5cm} 5 \hspace{1.5cm} 10 \hspace{1.5cm} 15$

Gly Thr Cys Gly Asp Ile Val Leu Ser Gln Ser Pro Ser Ser Leu Ala 20 25 30

Val Ser Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser 35 40 45

Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu Ala Trp Tyr Gln Gln 50 55 60

Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg 65 70 75 80

Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp 85 90 95

Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr $100 \hspace{1.5cm} 105 \hspace{1.5cm} 105 \hspace{1.5cm} 110 \hspace{1.5cm}$

Tyr Cys Thr Gln Ser Tyr Asn Leu Tyr Thr Phe Gly Gly Gly Thr Lys 115 120 125

Leu Glu Ile Lys 130

<210> 5 <211> 405

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<213> Humanized murine anti-human B7-2 heavy chain

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<210> 6 <211> 135 <212> PRT

<213> Humanized murine anti-human B7-2 heavy chain

<400> 6

Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe 35 40 45

Thr Asp Tyr Ala Ile Gln Trp Val Arg Gln Ala Pro Gly Gln Gly Leu 50 60

Glu Trp Ile Gly Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn 65 70 75 80

Gln Lys Phe Lys Gly Lys Ala Thr Met Thr Val Asp Lys Ser Thr Ser 85 90 95

Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val $100 \ \ 105 \ \ 110$

Tyr Tyr Cys Ala Arg Ala Ala Trp Tyr Met Asp Tyr Trp Gly Gl
n Gly 115 120 125

Thr Leu Val Thr Val Ser Ser 130 135

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      Humanized murine anti-human B7-2 light chain
<220>
<221>
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Met Asp Ser Gln Ala Gln Val Leu Ile Leu Leu Leu Trp Val Ser
age ace tot aga aac att ata eta aca caa tet eea aat tee eta get
Glv Thr Cvs Glv Asp Ile Val Leu Thr Gln Ser Pro Asp Ser Leu Ala
                                                    30
qta agc tta qqa qaq aqq qcc act att aqc tqc aaa tcc aqt caq aqt
144
Val Ser Leu Gly Glu Arq Ala Thr Ile Ser Cys Lys Ser Ser Gln Ser
                                                45
                            40
ctg ctc aac agt aga acc cga gag aac tac ttg gct tgg tac cag cag
192
Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu Ala Trp Tyr Gln Gln
aaa cca ggg cag cct cct aaa ctg ctg atc tac tgg gca tcc act agg
Lvs Pro Glv Gln Pro Pro Lvs Leu Leu Ile Tvr Trp Ala Ser Thr Arg
65
                                                             80
gaa tot ggg gto cot gat ogc tto agt ggc agt gga tot ggg aca gat
Glu Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
                85
                                    90
                                                        95
ttc act ctc acc atc agc agt ctg cag gct gaa gac gtg gca gtt tat
Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr
tac tgc acg caa tct tat aat ctt tac acg ttc gga cag ggg acc aag
384
Tyr Cys Thr Gln Ser Tyr Asn Leu Tyr Thr Phe Gly Gln Gly Thr Lys
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gtg gaa ata aaa 396 Val Glu Ile Lys 130 <210> 8 <211> 132 <212> PRT <213> Humanized murine anti-human B7-2 light chain <400> 8 20

Met Asp Ser Gln Ala Gln Val Leu Ile Leu Leu Leu Trp Val Ser

Gly Thr Cys Gly Asp Ile Val Leu Thr Gln Ser Pro Asp Ser Leu Ala 25 30

Val Ser Leu Gly Glu Arg Ala Thr Ile Ser Cys Lys Ser Ser Gln Ser 40

Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu Ala Trp Tyr Gln Gln 50 5.5 60

Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg 65 70 75 80

Glu Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp 85 90 95

Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr 100 105 110

Tyr Cys Thr Gln Ser Tyr Asn Leu Tyr Thr Phe Gly Gln Gly Thr Lys 115 120 125

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gat tat gct ata cag
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Asp Tyr Ala Ile Gln
1
               5
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<211> 5
<212> PRT
<213> Artificial Sequence
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<223> CDR1 of humanized murine anti-human B7-2 heavy chain
<400> 10
Asp Tyr Ala Ile Gln
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<210> 11
<211> 51
<212> DNA
<213> Artificial Sequence
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<223> CDR2 of humanized murine anti-human B7-2 heavy chain
<221> CDS
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gtt att aat att tac tat gat aat aca aac tac aac cag aag ttt aag
Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn Gln Lys Phe Lys
                5
ggc
51
Gly
<210> 12
<211> 17
<212> PRT
<213> Artificial Sequence
<220>
<223> CDR2 of humanized murine anti-human B7-2 heavy chain
<400> 12
Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn Gln Lys Phe Lys
                                                       15
Glv
<210> 13
<211> 21
<212> DNA
<213> Artificial Sequence
<220>
<223> CDR3 of humanized murine anti-human B7-2 heavy chain
<221> CDS
<222> (1)..(21)
<400> 13
geg gee tgg tat atg gae tac
21
Ala Ala Trp Tyr Met Asp Tyr
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<210> 14
<211> 7
<212> PRT
<213> Artificial Sequence
<220>
<223> CDR3 of humanized murine anti-human B7-2 heavy chain
<400> 14
Ala Ala Trp Tyr Met Asp Tyr
               5
<210> 15
<211> 51
<212> DNA
<213> Artificial Sequence
<220>
<223> CDR1 of humanized murine anti-human B7-2 light chain
<221> CDS
<222> (1)..(51)
<400> 15
aaa too agt cag agt ctg ctc aac agt aga acc cga gag aac tac ttg
Lys Ser Ser Gln Ser Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu
act
51
Ala
<210> 16
<211> 17
<212> PRT
<213> Artificial Sequence
<220>
<223> CDR1 of humanized murine anti-human B7-2 light chain
<400> 16
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Lys Ser Ser Gln Ser Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu
                                   10
Ala
<210> 17
<211> 21
<212> DNA
<213> Artificial Sequence
<220>
<223> CDR2 of humanized murine anti-human B7-2 light chain
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<222> (1)..(21)
<400> 17
tgg gca tcc act agg gaa tct
Trp Ala Ser Thr Arg Glu Ser
               5
<210> 18
<211> 7
<212> PRT
<213> Artificial Sequence
<220>
<223> CDR2 of humanized murine anti-human B7-2 light chain
<400> 18
Trp Ala Ser Thr Arg Glu Ser
               5
<210> 19
<211> 24
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<213> Artificial Sequence
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<220>

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<223> CDR3 of humanized murine anti-human B7-2 light chain
<221> CDS
<222> (1)..(24)
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acg caa tct tat aat ctt tac acg
2.4
Thr Gln Ser Tyr Asn Leu Tyr Thr
<210> 20
<211> 8
<212> PRT
<213> Artificial Sequence
<220>
<223> CDR3 of humanized murine anti-human B7-2 light chain
<400> 20
Thr Gln Ser Tyr Asn Leu Tyr Thr
<210> 21
<211> 405
<212> DNA
<213> Murine sp.
<220>
<221> CDS
<222> (1)..(405)
<223> Anti-B7-2 heavy chain
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Met Gly Trp Asn Cys Ile Ile Phe Phe Leu Val Thr Thr Ala Thr Gly
                  5
1
                                                         1.5
gtg cac tee cag gte cag etg cag tet ggg eet gag etg gtg agg
96
Val His Ser Gln Val Gln Leu Gln Gln Ser Glv Pro Glu Leu Val Arg
             20
                                 25
                                                     30
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cct ggg gaa tca gtg aag att tcc tgc aag ggt tcc ggc tac aca ttc 144
Pro Gly Glu Ser Val Lys Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe 35 40 45

act gat tat gct ata cag tgg gtg aag cag agt cat gca aag agt cta 192

gag tgg att gga gtt att aat att tac tat gat aat aca aac tac aac 240 Glu Trp Ile Gly Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn 65 70 75 80

cag aag ttt aag ggc aag gcc aca atg act gta gac aaa tcc tcc agc 288
Gln Lys Phe Lys Gly Lys Ala Thr Met Thr Val Asp Lys Ser Ser Ser 85 90 95

aca gcc tat atg gaa ctt gcc aga ttg aca tct gag gat tct gcc atc 336 Thr Ala Tyr Met Glu Leu Ala Arg Leu Thr Ser Glu Asp Ser Ala Ile 100 105 110

tat tac tgt gca aga gcg gcc tgg tat atg gac tac tgg ggt caa gga 384 Tyr Tyr Cys Ala Arg Ala Ala Trp Tyr Met Asp Tyr Trp Gly Gln Gly 115 120 125

acc tca gtc acc gtc tcc tca 405 Thr Ser Val Thr Val Ser Ser

Thr Ser Val Thr Val Ser Ser 130 135

<210> 22 <211> 135

VZ11/ 133

<212> PRT

<213> Murine sp.

<220>

<223> Anti-B7-2 heavy chain

<400> 22

Met Gly Trp Asn Cys Ile Ile Phe Phe Leu Val Thr Thr Ala Thr Gly 5 15 Val His Ser Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Arq Pro Gly Glu Ser Val Lys Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe 40 45 Thr Asp Tyr Ala Ile Gln Trp Val Lys Gln Ser His Ala Lys Ser Leu 50 55 60 Glu Trp Ile Gly Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn 65 80 Gln Lys Phe Lys Gly Lys Ala Thr Met Thr Val Asp Lys Ser Ser Ser 85 90 95 Thr Ala Tyr Met Glu Leu Ala Arg Leu Thr Ser Glu Asp Ser Ala Ile Tyr Tyr Cys Ala Arg Ala Ala Trp Tyr Met Asp Tyr Trp Gly Gln Gly 115 Thr Ser Val Thr Val Ser Ser <210> 23 <211> 396 <212> DNA <213> Murine sp. <220> <221> CDS <222> (1)..(396) <223> Anti-B7-2 light chain <400> 23 atg gat toa cag goo cag gtt ctt ata ttg ctg ctg cta tgg gta tct Met Asp Ser Gln Ala Gln Val Leu Ile Leu Leu Leu Trp Val Ser ggt acc tgt ggg gac att gtg ctg tca cag tct cca tcc tcc ctg gct 96

Glv Thr Cvs Glv Asp Ile Val Leu Ser Gln Ser Pro Ser Ser Leu Ala gtg tca gca gga gag aag gtc act atg agc tgc aaa tcc agt cag agt 144 Val Ser Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser 40 ctg ctc aac agt aga acc cga gag aac tac ttg gct tgg tac cag cag 192 Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu Ala Trp Tyr Gln Gln 60 aaa cca ggg cag tot cot aaa ctg ctg atc tac tgg gca toc act agg 240 Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg 65 80 gaa tot ggg gto oot gat ogc tto aca ggo agt gga tot ggg aca gat 288 Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp 85 95 90 ttc act ctc acc atc agc agt gtg cag gct gaa gac ctg gca gtt tat Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr tac tgc acg caa tct tat aat ctt tac acg ttc gga ggg ggg acc aag Tyr Cys Thr Gln Ser Tyr Asn Leu Tyr Thr Phe Gly Gly Gly Thr Lys 115 ctg gaa ata aaa 396 Leu Glu Ile Lys 130 <210> 24 <211> 132

<212> PRT <213> Murine sp.

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<220> <223> Anti-B7-2 light chain

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Gly Thr Cys Gly Asp Ile Val Leu Ser Gln Ser Pro Ser Ser Leu Ala
             20
                                 25
Val Ser Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser
                             40
Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu Ala Trp Tyr Gln Gln
Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg
 65
Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp
                 85
                                      90
Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tvr
            100
                                105
Tyr Cys Thr Gln Ser Tyr Asn Leu Tyr Thr Phe Gly Gly Gly Thr Lys
        115
                            120
                                                125
Leu Glu Ile Lys
    130
<210> 25
<211> 405
<212> DNA
<213> Artificial Seguence
<220>
<223> Description of Artificial Sequence: Humanized
      murine anti-human B7-2 heavy chain
<220>
<221> CDS
<222> (1)..(405)
<400> 25
atg ggt tgg aac tgt atc atc ttc ttt ctg gtt acc aca gct aca ggt
48
Met Gly Trp Asn Cys Ile Ile Phe Phe Leu Val Thr Thr Ala Thr Gly
                                                          15
                                     10
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gtg cac tee cag gte cag etg gtg cag tet ggg get gag gtg aag aag 96 Val His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys cct ggg age tea gtg aag gtg tee tge aaa get tee gge tae aca tte 144 Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe act gat tat gct ata cag tgg gtg aga cag gct cct gga cag ggc ctc 192 Thr Asp Tvr Ala Ile Gln Trp Val Arg Gln Ala Pro Glv Gln Glv Leu 60 gag tgg att gga gtt att aat att tac tat gat aat aca aac tac aac 240 Glu Trp Ile Gly Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn 75 80 65 cag aag ttt aag ggc aag gcc aca atg act gta gac aag tcg acg agc Gln Lys Phe Lys Gly Lys Ala Thr Met Thr Val Asp Lys Ser Thr Ser 85 90 95 aca gcc tat atg gaa ctt agt tct ttg aga tct gag gat acg gcc gtt Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val tat tac tgt gca aga gcg gcc tgg tat atg gac tac tgg ggt caa ggt 384 Tyr Tyr Cys Ala Arg Ala Ala Trp Tyr Met Asp Tyr Trp Gly Gln Gly 120 acc ctt gtc acc gtc tcc tca 405 Thr Leu Val Thr Val Ser Ser

<210> 26

<211> 135

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Humanized murine anti-human B7-2 heavy chain

<400> 26

Met Gly Trp Asn Cys Ile Ile Phe Phe Leu Val Thr Thr Ala Thr Gly
1 5 10 15

Val His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
20 25 30

Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe $35 \hspace{1cm} 40 \hspace{1cm} 45$

Thr Asp Tyr Ala Ile Gln Trp Val Arg Gln Ala Pro Gly Gln Gly Leu 50 55 60

Glu Trp Ile Gly Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn 65 70 75 80

Gln Lys Phe Lys Gly Lys Ala Thr Met Thr Val Asp Lys Ser Thr Ser \$85\$ 90 95

Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val $100 \hspace{1.5cm} 105 \hspace{1.5cm} 110 \hspace{1.5cm}$

Thr Leu Val Thr Val Ser Ser 130 135

<210> 27

<211> 396

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Humanized murine anti-human B7-2 light chain

<220>

<221> CDS

<222> (1)..(396)

<400> 27

atg gat tea eag gee eag gtt ett ata ttg etg etg eta tgg gta tet 48

Met Asp Ser Gln Ala Gln Val Leu Ile Leu Leu Leu Leu Trp Val Ser $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$

ggc acc tgt ggg gac att gtg ctg aca cag tct cca gat tcc ctg gct

Gly Thr Cys Gly Asp Ile Val Leu Thr Gln Ser Pro Asp Ser Leu Ala 20 25 30

gta agc tta gga gag agg gcc act att agc tgc aaa tcc agt cag agt 144

Val Ser Leu Gly Glu Arg Ala Thr Ile Ser Cys Lys Ser Ser Gln Ser
35 40 45

ctg ctc aac agt aga acc cga gag aac tac ttg gct tgg tac cag cag 192 Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu Ala Trp Tyr Gln Gln 50 55 60

aaa cca ggg cag cct cct aaa ctg ctg atc tac tgg gca tcc act agg 240

Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg 65 70 75 80

gaa tot ggg gto oot gat ogo tto agt ggc agt gga tot ggg aca gat 288 Glu Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp

90

95

ttc act ctc acc atc agc agt ctg cag gct gaa gac gtg gca gtt tat 336 Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr

tac tgc acg caa tot tat aat ott tac acg ttc gga cag ggg acc aag 384 Tyr Cys Thr Gln Ser Tyr Asn Leu Tyr Thr Phe Gly Gln Gly Thr Lys

gtg gaa ata aaa 396 Val Glu Ile Lys <211> 132

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Humanized murine anti-human B7-2 light chain

<400> 28

Met Asp Ser Gln Ala Gln Val Leu Ile Leu Leu Leu Leu Trp Val Ser $1 \hspace{1.5cm} 5 \hspace{1.5cm} 10 \hspace{1.5cm} 15$

Gly Thr Cys Gly Asp Ile Val Leu Thr Gln Ser Pro Asp Ser Leu Ala $20 \hspace{1.5cm} 25 \hspace{1.5cm} 30$

Val Ser Leu Gly Glu Arg Ala Thr Ile Ser Cys Lys Ser Ser Gln Ser 35 40 45

Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu Ala Trp Tyr Gln Gln 50 55 60

Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg 65 70 75 80

Glu Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp $85 \\ 90 \\ 95$

Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr 100 105 110

Tyr Cys Thr Gln Ser Tyr Asn Leu Tyr Thr Phe Gly Gln Gly Thr Lys 115 120 125

Val Glu Ile Lys 130

<210> 29

<211> 15

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: CDR1 of humanized murine anti-human B7-2 heavy chain

<220>

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<221> CDS
<222> (1)..(15)
<400> 29
gat tat gct ata cag
15
Asp Tyr Ala Ile Gln
<210> 30
<211> 5
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: CDR1 of humanized
      murine anti-human B7-2 heavy chain
<400> 30
Asp Tyr Ala Ile Gln
 1
<210> 31
<211> 51
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: CDR2 of
      humanized murine anti-human B7-2 heavy chain
<220>
<221> CDS
<222> (1)..(51)
<400> 31
gtt att aat att tac tat gat aat aca aac tac aac cag aag ttt aag
Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn Gln Lys Phe Lys
                  5
                                                          1.5
ggc
51
Glv
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<210> 32
<211> 17
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: CDR2 of humanized
      murine anti-human B7-2 heavy chain
<400> 32
Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn Gln Lys Phe Lys
Gly
<210> 33
<211> 21
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: CDR3 of
      humanized murine anti-human B7-2 heavy chain
<220>
<221> CDS
<222> (1)..(21)
<400> 33
gcg gcc tgg tat atg gac tac
21
Ala Ala Trp Tyr Met Asp Tyr
<210> 34
<211> 7
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: CDR3 of humanized
      murine anti-human B7-2 heavy chain
<400> 34
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Ala Ala Trp Tyr Met Asp Tyr
 1
<210> 35
<211> 51
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: CDR1 of
      humanized murine anti-human B7-2 light chain
<220>
<221> CDS
<222> (1)..(51)
<400> 35
aaa tee agt cag agt ctg etc aac agt aga acc ega gag aac tac ttg
Lys Ser Ser Gln Ser Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu
                  5
                                                          15
gct
51
Ala
<210> 36
<211> 17
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: CDR1 of humanized
      murine anti-human B7-2 light chain
<400> 36
Lys Ser Ser Gln Ser Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu
 1
                                                          15
Ala
<210> 37
<211> 21
<212> DNA
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<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: CDR2 of
      humanized murine anti-human B7-2 light chain
<220>
<221> CDS
<222> (1)..(21)
<400> 37
tqq qca tcc act agg gaa tct
Trp Ala Ser Thr Arg Glu Ser
<210> 38
<211> 7
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: CDR2 of humanized
      murine anti-human B7-2 light chain
<400> 38
Trp Ala Ser Thr Arg Glu Ser
<210> 39
<211> 24
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: CDR3 of
      humanized murine anti-human B7-2 light chain
<220>
<221> CDS
<222> (1)..(24)
<400> 39
acq caa tot tat aat ott tac acg
24
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Thr Gln Ser Tyr Asn Leu Tyr Thr
 1
                  5
<210> 40
<211> 8
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: CDR3 of humanized
      murine anti-human B7-2 light chain
<400> 40
Thr Gln Ser Tyr Asn Leu Tyr Thr
                5
<210> 41
<211> 1960
<212> DNA
<213> Mus sp.
<220>
<221> CDS
<222> (12)..(408)
<220>
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<222> (768)..(1087)
<400> 41
totagaccae c atg gat toa cag goo cag gtt ott ata ttg otg ota
50
             Met Asp Ser Gln Ala Gln Val Leu Ile Leu Leu Leu Leu
               1
                               5
tgg qta tct ggc acc tgt ggg gac att gtg ctg aca cag tct cca gat
98
Trp Val Ser Gly Thr Cys Gly Asp Ile Val Leu Thr Gln Ser Pro Asp
    15
```

tcc ctg gct gta agc tta gga gag agg gcc act att agc tgc aaa tcc 146 Ser Leu Ala Val Ser Leu Glv Glu Arg Ala Thr Ile Ser Cvs Lvs Ser

40

45

30

agt cag agt ctg ctc aac agt aga acc cga gag aac tac ttg gct tgg 194

Ser Gln Ser Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu Ala Trp $50 \ 55 \ 60$

tac cag cag aaa cca ggg cag cct cct aaa ctg ctg atc tac tgg gca 242

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala 657075

tcc act agg gaa tct ggg gtc cct gat cgc ttc agt ggc agt gga tct 290 Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser 80 85 90

ggg aca gat ttc act ctc acc atc agc agt ctg cag gct gaa gac gtg 338 Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val

100

gca gtt tat tac tgc agc caa tct tat aat ctt tac acg ttc gga cag 386

Ala Val Tyr Tyr Cys Ser Gln Ser Tyr Asn Leu Tyr Thr Phe Gly Gln 110 125

ggg acc aag gtg gaa ata aaa c gtaagtagte tteteaacte tagaaattet 438

Gly Thr Lys Val Glu Ile Lys

95

aaactetgag ggggteggat gaegtggeea ttetttgeet aaageattga gtttaetgea 498

aggtcagaaa agcatgcaaa gccctcagaa tggctgcaaa gagctccaac aaaacaattt 558

agaactttat taaggaatag ggggaagcta ggaagaaact caaaacatca agattttaaa 618

tacgettett ggteteettg etataattat etgggataag eatgetgttt tetgtetgte 678

cctaacatgc cctgtgatta tccgcaaaca acacacccaa gggcagaact ttgttactta 738

aacaccatcc tgtttgcttc tttcctcag ga act gtg gct gca cca tct gtc 790

Arg Thr Val Ala Ala Pro Ser Val 135 140

ttc atc ttc ccg cca tct gat gag cag ttg aaa tct gga act gcc tct $838\,$

Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser 145 150 155

gtt gtg tgc ctg ctg aat aac ttc tat ccc aga gag gcc aaa gta cag 886

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln
160 165 170

tgg aag gtg gat aac gcc ctc caa tcg ggt aac tcc cag gag agt gtc 934 Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val 175 180 185

aca gag cag gac agc aag gac agc acc tac agc ctc agc agc acc ctg 982 Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu 190 195 200

acg ctg agc aaa gca gac tac gag aaa cac aaa gtc tac gcc tgc gaa 1030

Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu 205 210210215

gtc acc cat cag ggc ctg agc tcg ccc gtc aca aag agc ttc aac agg 1078

Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg 225 230 235

gga gag tgt tagagggaga agtgccccca cctgctcctc agttccagcc 1127 Gly Glu Cys

 ${\tt tgaccccctc}\ {\tt ccatcctttg}\ {\tt gcctctgacc}\ {\tt ctttttccac}\ {\tt aggggaccta}\ {\tt cccctattgc}\ {\tt 1187}$

ggtcctccag ctcatctttc acctcacccc cctcctcctc cttggcttta attatgctaa 1247

tgttggagga gaatgaataa ataaagtgaa tetttgeace tgtggtttet etettteete 1307

atttaataat tattatotgt tgttttacca actactcaat ttotottata agggactaaa 1367

tatgtagtca toctaaggog cataaccatt tataaaaaatc atcettcatt ctattttacc 1427

ctatcatcct ctgcaagaca gtcctccctc aaacccacaa gccttctgtc ctcacagtcc 1487

cctgggccat ggtaggagag acttgcttcc ttgttttccc ctcctcagca agccctcata 1547

 $\tt gtccttttta \ agggtgacag \ gtcttacagt \ catatatcct \ ttgattcaat \ tccctgggaa \ 1607$

tcaaccaaag caaatttttc aaaagaagaa acctgctata aagagaatca ttcattgcaa 1667

catgatataa aataacaaca caataaaagc aattaaataa acaaacaata gggaaatgtt 1727

taagttcatc atggtactta gacttaatgg aatgtcatgc cttatttaca tttttaaaca 1787

ggtactgagg gactcctgtc tgccaagggc cgtattgagt actttccaca acctaattta 1847

atocacacta tactgtgaga ttaaaaacat tcattaaaat gttgcaaagg ttctataaag 1907

ctgagagaca aatatattot ataactcago aatcccactt ctaggatcaa tto $1\,960$

<210> 42

<211> 239

<212> PRT

<213> Mus sp.

<400> 42

Met Asp Ser Gln Ala Gln Val Leu Ile Leu Leu Leu Leu Trp Val Ser

Gly Thr Cys Gly Asp Ile Val Leu Thr Gln Ser Pro Asp Ser Leu Ala 20 25 30 Val Ser Leu Gly Glu Arg Ala Thr Ile Ser Cys Lys Ser Ser Gln Ser 35 45 Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu Ala Trp Tyr Gln Gln 50 55 60 Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg 70 65 8.0 Glu Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp 85 90 95 Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Ser Gln Ser Tyr Asn Leu Tyr Thr Phe Gly Gln Gly Thr Lys 115 125 Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro 130 135 140 Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu 145 160 Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp 165 175 Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp 180 185 190

Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys 195 200 205

Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln 210 215 220

Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys 225 230 235

<210> 43

<211> 2249

<212> DNA

<213> Mus sp.

<220>

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<222> (12)..(417)
<220>
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<222> (655)..(948)
<221> CDS
<222> (1341)..(1376)
<220>
<221> CDS
<222> (1495)..(1821)
<220>
<221> CDS
<222> (1919)..(2238)
<400> 43
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50
             Met Gly Trp Asn Cys Ile Ile Phe Phe Leu Val Thr Thr
gct aca ggt gtg cac tcc cag gtc cag ctg gtg cag tct ggg gct gag
98
Ala Thr Gly Val His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu
gtg aag aag oot ggg ago toa gtg aag gtg too tgc aaa got too ggo
Val Lvs Lvs Pro Glv Ser Ser Val Lvs Val Ser Cvs Lvs Ala Ser Glv
30
                     35
                                          40
                                                              45
tac aca ttc act gat tat gct ata cag tgg gtg aga cag gct cct gga
Tyr Thr Phe Thr Asp Tyr Ala Ile Gln Trp Val Arg Gln Ala Pro Gly
                 50
                                                          60
cag ggc ctc gag tgg att gga gtt att aat att tac tat gat aat aca
242
Gln Gly Leu Glu Trp Ile Gly Val Ile Asn Ile Tyr Tyr Asp Asn Thr
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aac tac aac cag aag ttt aag ggc aag gcc aca atg act gta gac aag

<221> CDS

290

Asn Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Met Thr Val Asp Lys 80 85 90

tog acg age aca gee tat atg gaa ett agt tet ttg aga tet gag gat 338

Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp $95 \hspace{1.5cm} 100 \hspace{1.5cm} 105 \hspace{1.5cm}$

acg goe gtt tat tac tgt goa aga gog goe tgg tat atg gae tac tgg 386

ggt caa ggt acc ctt gtc acc gtc tcc tca g gtgagtcett aaaacctcta 437

Gly Gln Gly Thr Leu Val Thr Val Ser Ser 130 135

gagetttetg gggegageeg ggeetgaett tggetttggg geagggagtg ggetaaggtg 497

aggcaggtgg cgccagccag gtgcacaccc aatgcccgtg agcccagaca ctggaccctg 557

cctggaccct cgtggataga caagaaccga ggggcctctg cgccctgggc ccagctctgt 617

cccacaccgc ggtcacatgg caccacctct cttgcag cc tcc acc aag ggc cca $671\,$

Ala Ser Thr Lys Gly Pro 140

teg gtc ttc ccc ctg gcg ccc tgc tcc agg agc acc tcc gag agc aca 719

Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr $145 \hspace{1.5cm} 150 \hspace{1.5cm} 155$

gog god etg gge tge etg gte aag gae tae tte eee gaa eeg gtg aeg 767

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr 160 165 170

gtg tog tgg aac toa ggc gct ctg acc agc ggc gtg cac acc ttc cca 815 Val Sar Tro Ben Sar Cly Bla Leu Thr Sar Cly Val Hie Thr Pha Pro

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro 175 180 185 get gte eta cag tee tea gga ete tae tee ete age age gtg gtg ace 863 Ala Val Leu Gln Ser Ser Glv Leu Tvr Ser Leu Ser Ser Val Val Thr

Ala Val Leu Gin Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr 190 195 200 205

gtg ccc tcc agc aac ttc ggc acc cag acc tac acc tgc aac gta gat 911

Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp 210 215 220

cac aag ccc agc aac acc aag gtg gac aag aca gtt g gtgagaggcc 958 His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val

ageteaggga gggagggtgt etgetggaag ceaggeteag eeeteetgee tggaegeace 1018

coggetgtgc agecccagec cagggeagea aggeaggeec catetgtete etcaccegga 1078

ggcctctgcc cgccccactc atgctcaggg agagggtctt ctggcttttt ccaccaggct 1138

ccaggcaggc acaggctggg tgcccctacc ccaggccctt cacacacagg ggcaggtgct 1198

tggctcagac ctgccaaaag ccatatccgg gaggaccctg cccctgacct aagccgaccc 1258

caaaggccaa actgtccact ccctcagctc ggacaccttc tctcctccca gatccgagta

actoccaato ttotototgo ag ag ogo aaa tgt tgt gto gag tgo oca oog 1369

Glu Arg Lys Cys Cys Val Glu Cys Pro Pro 235 240

tgc cca g gtaagecage ccaggeeteg ceetecaget caaggeggga caggtgeeet 1426

Cys Pro

245

agagtageet geatecaggg acaggeecea getgggtget gacaegteea cetecatete 1486

ttcctcaq	g ca	сса	cct	gcg	gca	gca	ccg	tca	gtc	ttc	ctc	ttc	ccc	cca
	Ala	Pro	Pro	Ala	Ala 250	Ala	Pro	Ser	Val	Phe 255	Leu	Phe	Pro	Pro
aaa ccc 1583	aag	gac	acc	ctc	atg	atc	tcc	cgg	acc	cct	gag	gtc	acg	tgc
Lys Pro 260	Lys	Asp	Thr	Leu 265	Met	Ile	Ser	Arg	Thr 270	Pro	Glu	Val	Thr	Cys 275
gtg gtg 1631	gtg	gac	gtg	agc	cac	gaa	gac	ccc	gag	gtc	cag	ttc	aac	tgg
Val Val	Val	Asp	Val 280	Ser	His	Glu	Asp	Pro 285	Glu	Val	Gln	Phe	Asn 290	Trp

tac gtg gac ggc gtg gag gtg cat aat gcc aag aca aag cca cgg gag 1679 Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu

295 300 305

gag cag ttc aac agc acg ttc cgt gtg gtc agc gtc ctc acc gtt gtg 1727 Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser Val Leu Thr Val Val 310 320

cac cag gac tgg ctg aac ggc aag gag tac aag tgc aag gtc tcc aac 1775 His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn 325 330 335

aaa ggc ctc cca gcc ccc atc gag aaa acc atc tcc aaa acc aaa g 1821 Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys 340 345 350

gtgggacccg cggggtatga gggccacatg gacagaggcc ggctcggccc accctctgcc 1881

ctgggagtga ccgctgtgcc aacctctgtc cctacag gg cag ccc cga gaa cca 1935

> Gly Gln Pro Arg Glu Pro 355 360

cag gtg tac acc ctg ccc cca tcc cgg gag gag atg acc aag aac cag 1983 Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln 365 370 375 gte age etg ace tge etg gte aaa gge t
te tae eee age gae ate gee $2031\,$

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala 380 385 390

gtg gag tgg gag agc aat ggg cag ccg gag aac aac tac aag acc aca 2079

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr 395 400 405

cet ecc atg etg gae tee gae gge tee tte tte etc tae age aag etc 2127

Pro Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu 410 415 420

acc gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca tgc tcc 2175

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser 425 430430435440

gtg atg cat gag gct ctg cac aac cac tac acg cag aag agc ctc tcc 2223

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser 445 450 450

ctg tcc ccg ggt aaa tgagtgaatt c 2249 Leu Ser Pro Gly Lys 460

<210> 44 <211> 461 <212> PRT

<213> Mus sp.

<400> 44

Met Gly Trp Asn Cys Ile Ile Phe Phe Leu Val Thr Thr Ala Thr Gly
1 10 15

Val His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys 20 25 30

Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe 35 40 45

Thr	Asp 50	Tyr	Ala	Ile	Gln	Trp 55	Val	Arg	Gln	Ala	Pro 60	Gly	Gln	Gly	Leu
Glu 65	Trp	Ile	Gly	Val	Ile 70	Asn	Ile	Tyr	Tyr	Asp 75	Asn	Thr	Asn	Tyr	Asn 80
Gln	Lys	Phe	Lys	Gly 85	Lys	Ala	Thr	Met	Thr 90	Val	Asp	Lys	Ser	Thr 95	Ser
Thr	Ala	Tyr	Met 100	Glu	Leu	Ser	Ser	Leu 105	Arg	Ser	Glu	Asp	Thr 110	Ala	Val
Tyr	Tyr	Cys 115	Ala	Arg	Ala	Ala	Trp 120	Tyr	Met	Asp	Tyr	Trp 125	Gly	Gln	Gly
Thr	Leu 130	Val	Thr	Val	Ser	Ser 135	Ala	Ser	Thr	Lys	Gly 140	Pro	Ser	Val	Phe
Pro 145	Leu	Ala	Pro	Cys	Ser 150	Arg	Ser	Thr	Ser	Glu 155	Ser	Thr	Ala	Ala	Leu 160
Gly	Cys	Leu	Val	Lys 165	Asp	Tyr	Phe	Pro	Glu 170	Pro	Val	Thr	Val	Ser 175	Trp
Asn	Ser	Gly	Ala 180		Thr					Thr			Ala 190	Val	Leu

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser

Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp His Lys Pro

Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys Cys Val Glu

Cys Pro Pro Cys Pro Ala Pro Pro Ala Ala Ala Pro Ser Val Phe Leu

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Gln

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys

Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser Val Leu 305 310 315 320 Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys 325 330 Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys 340 345 350 Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser 355 360 365 Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys 380 Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln 385 390 395 400 Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp Ser Asp Gly 405 410 Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln 420 425 Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn 435 440 445 His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys 460 <210> 45 <211> 327 <212> DNA <213> Homo sapiens <400> 45 gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc

gggaaagtte etaageteet gatetatget geateeaett tgeaateagg ggteeeatet $180\,$

atcacttqcc qqqcqaqtca qqqcattaqc aattatttaq cctqqtatca qcaqaaacca

60

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cggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag cctgcagcct
240
qaaqatqttq caacttatta ctqtcaaaaq tataacaqtq cccctccqaq tacqttcqqc
300
caagggacca aggtggaaat caaacgt
327
<210> 46
<211> 339
<212> DNA
<213> Homo sapiens
<400> 46
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atcaactqca aqtccaqcca qaqtqtttta tacaqctcca acaacaaqaa ttacttaact
tggtaccagc agaaaccagg acagcetect aagetgetea tttactggge atctaccegg
qaatccqqqq tccctqaccq attcaqtqqc aqcqqqtctq qqacaqattt cactctcacc
240
atcagcagcc tgcaggctga agatgtggca gtttattact gtcagcaata ttatagtact
300
cctcgaacgt tcggccaagg gaccaaggtg gaaatcaaa
339
<210> 47
<211> 95
<212>
      PRT
<213>
      Homo sapiens
<400> 47
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Asn Tyr 20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile $35 \hspace{1.5cm} 40 \hspace{1.5cm} 45 \hspace{1.5cm}$

Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro 65 70 75 80

Glu Asp Val Ala Thr Tyr Tyr Cys Gln Lys Tyr Asn Ser Ala Pro $85 \hspace{0.25in} 90 \hspace{0.25in} 95$

<210> 48

<211> 101 <212> PRT

<213> Homo sapiens

<400> 48

Asp Ile Gln Leu Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Tyr Ser $20 \hspace{1.5cm} 25 \hspace{1.5cm} 30 \hspace{1.5cm}$

Ser Asn Asn Lys Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln Pro 35 40 45

Pro Lys Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val $50 \hspace{1cm} 55 \hspace{1cm} 60 \hspace{1cm}$

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr 65 70 75 80

Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln 85 90 95

Tyr Tyr Ser Thr Pro 100

<210> 49

<211> 368

<212> DNA

<213> Homo sapiens

<400> 49

aggtgcaget ggtgcagtet ggggctgagg tgaagaagee tgggteeteg gtaaaggtet $60\,$

 $\verb|cctgcaaggc| ttctggaggc| accttcagta| gttatactat| cagctgggtg| cgacaggccc| 120$

ctggacaagg gettgagtgg atgggaagga teatgeetat eettggacta geaaattaeg 180

cacagaagtt ccagggcaga gtcacgatta ccgcggacaa atccacgagc acagcctaca 240

tggagctgag cagcctgaga tctgaggaca cggccgtgta ttactgtgcg agagatcccg 300

attatgtttg ggggagcgac aactggttcg acccctgggg ccagggaacc ctgctcatcg 360

tctcctca 368

<210> 50

<211> 358

<212> DNA

<213> Homo sapiens

<400> 50

gtgcagctgg tggagtctgg gggaggcttg gtcaagcctg gagggtccct gagactctcc 60

tgtgcagect eggatteace tttactagga atectaegag etgggtaege eaggeteeag 120

ggaaggggct ggagtgggtg gttaatataa tggtagtcgg aattgaacca tactatgcgg 180

actotytyaa gygccgatto accatotooa gaggcaacgo caagaactoa ctytatotyo $240\,$

aaatgaacag cotgagagco gaggacacgg cogtgtatta ctgtgcgaga gggatctgtc 300

ttatgacaga ggctactttg actactgggg ccagggaacc ctggtcaccg tctcctca 358

<210> 51

<211> 97

<212> PRT

<213> Homo sapiens

<400> 51

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser Ser $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$

Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr Thr 20 25 30

Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly 35 40 45

Arg Ile Met Pro Ile Leu Gly Leu Ala Asn Tyr Ala Gln Lys Phe Gln 50 55 60

Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr Met 65 70 75 80

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala 85 90 95

Arq

<210> 52 <211> 98 <212> PRT

<213> Homo sapiens

<400> 52

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr Tyr $20 \hspace{1.5cm} 25 \hspace{1.5cm} 30 \hspace{1.5cm}$

Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser 35 40 45

Tyr Ile Ser Ser Arg Gly Ser Glu Thr Ile Tyr Tyr Ala Asp Ser Val $50 \hspace{1.5cm} 55 \hspace{1.5cm} 60$

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr $65 70 75 80 $

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys 85 90 95

Ala Arg